

BREAST CANCER IMMUNOTHERAPY, COVID-19 & SPACE SCIENCE

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July 8th, 2020



HOUSTON METHODIST RESEARCH INSTITUTE

DEPARTMENT OF NANOMEDICINE

HOUSTON
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LEADING MEDICINE

TEXAS MEDICAL CENTER



Houston Methodist Research Institute

- Hospital-based
- 10-year old
- Conceived for translational research

Department of Nanomedicine

Total Personnel: 119

Faculty: 12

Research Associates, PhD: 29

Graduate & Undergraduate Students: 45

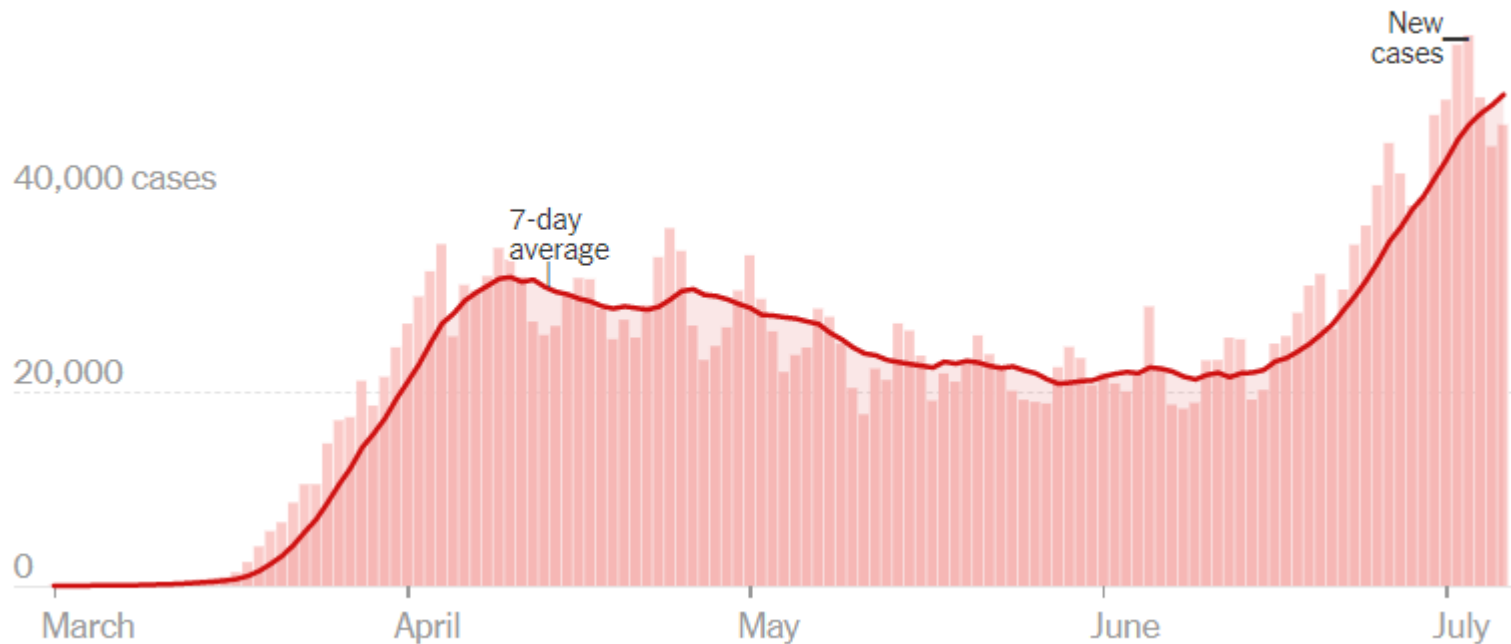
Research Assistants: 26

Admin Staff: 7

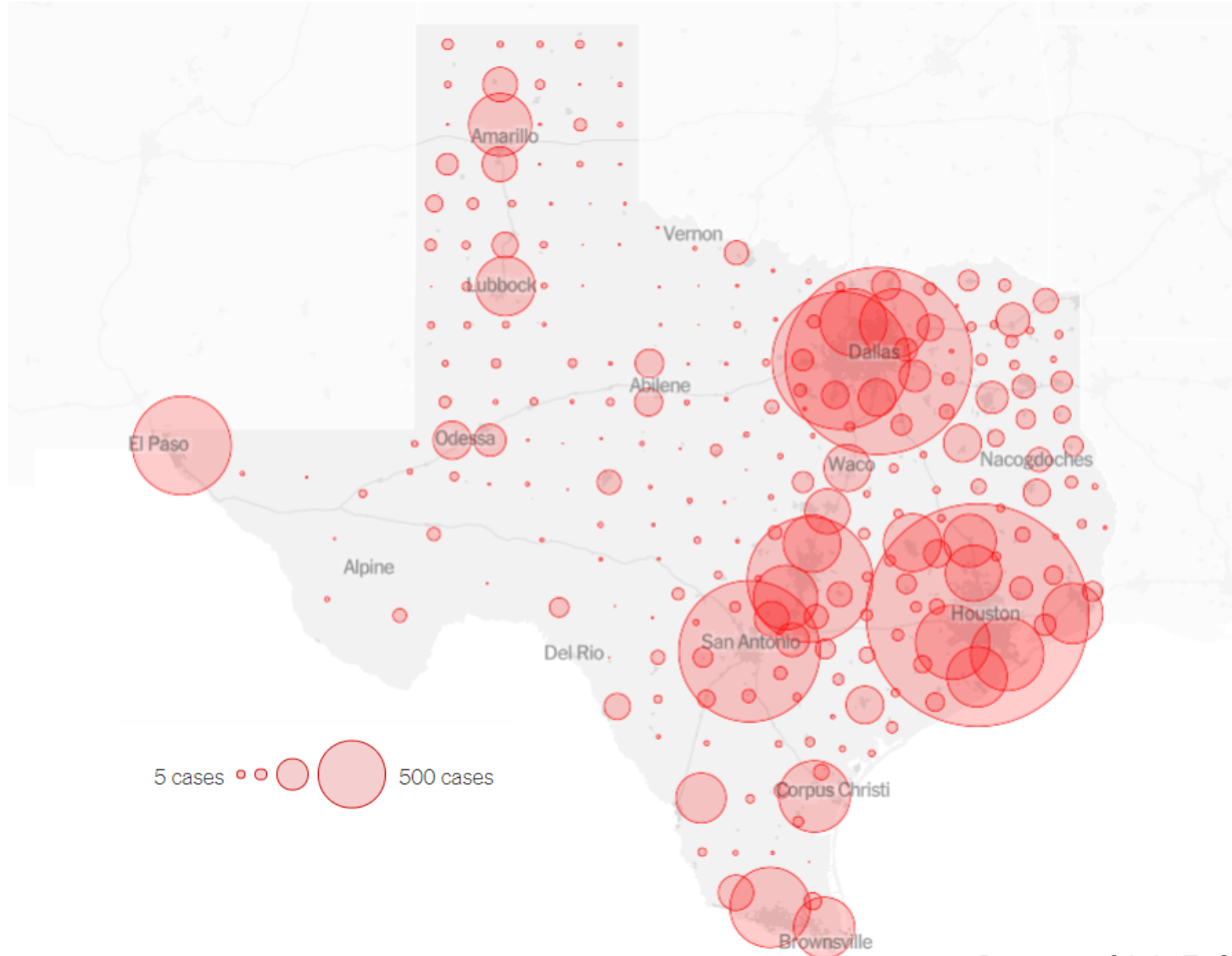


NEW CASES ANNOUNCED EACH DAY

New reported cases by day in the United States



TEXAS SPREAD: CONFIRMED CASES BY COUNTY

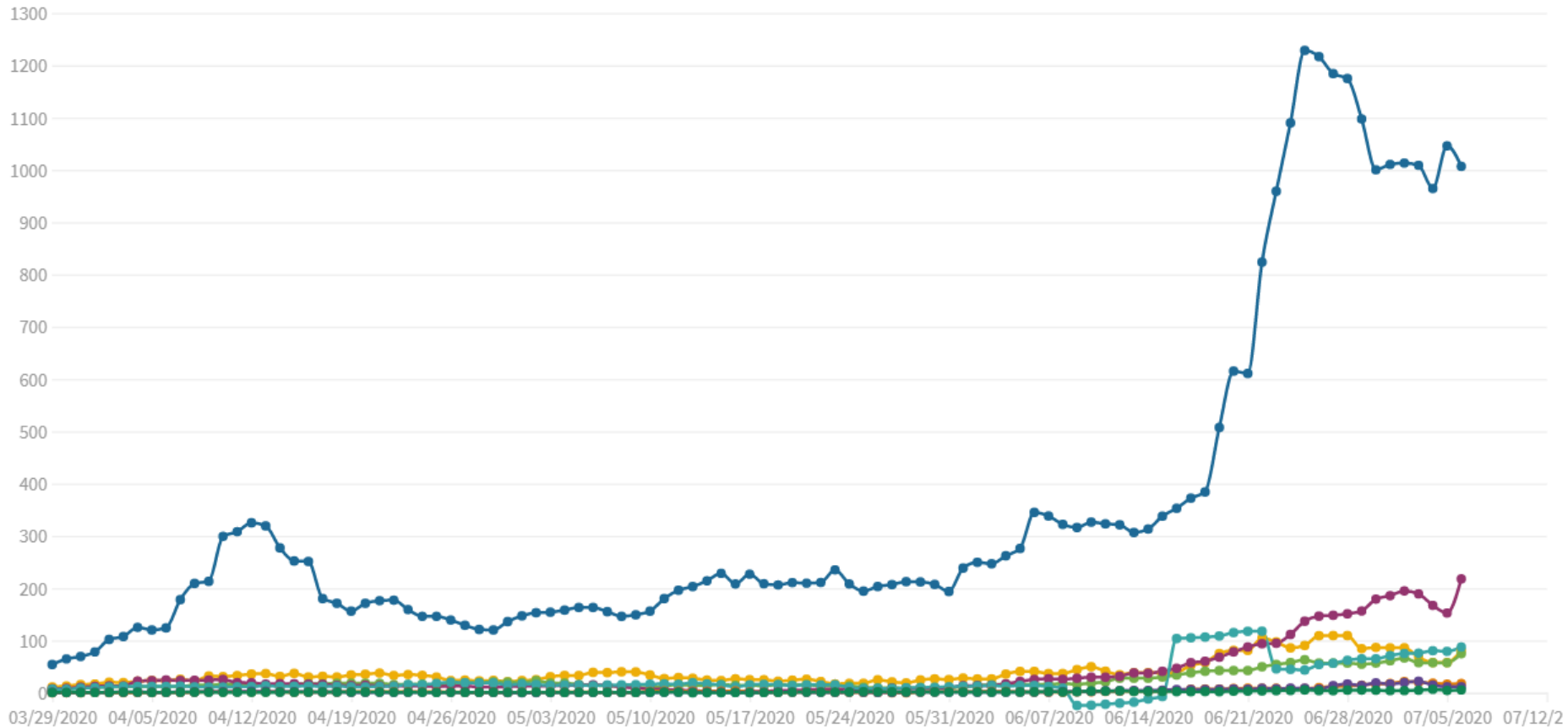


Data as of July 7, 2020

NEW CASES BY COUNTY

Seven-day rolling average of new cases for each county in the Houston region

■ Harris ■ Fort Bend ■ Montgomery ■ Galveston ■ Brazoria ■ Liberty ■ Chambers ■ Waller



Source: Texas Department of State Health Services, Hearst Newspaper reporting • On June 9, Brazoria removed TCDJ cases and deaths from their reports, which removed 2 deaths and 220 cases from the region total. By Jordan Rubio

IMPACT OF COVID-19 VS NORDIC COUNTRIES



SWEDEN



DENMARK



NORWAY



FINLAND

REPORTED DEATHS

5,433

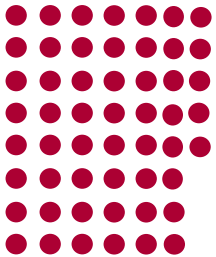
607

251

329

DEATHS PER 100K RESIDENTS

53



10



5



6



REPORTED CASES

73,061

13,079

8,936

7,257

CASES PER 100K

714

227

151

137

Comparison – Deaths per 100k Population:

- Harris County: 9
- United States: 39.82
- New York City: 269
- Orleans Parish: 137
- Wayne, MI: 156

How does a society determine the morally and ethically “acceptable” death rate when balanced against economic viability?

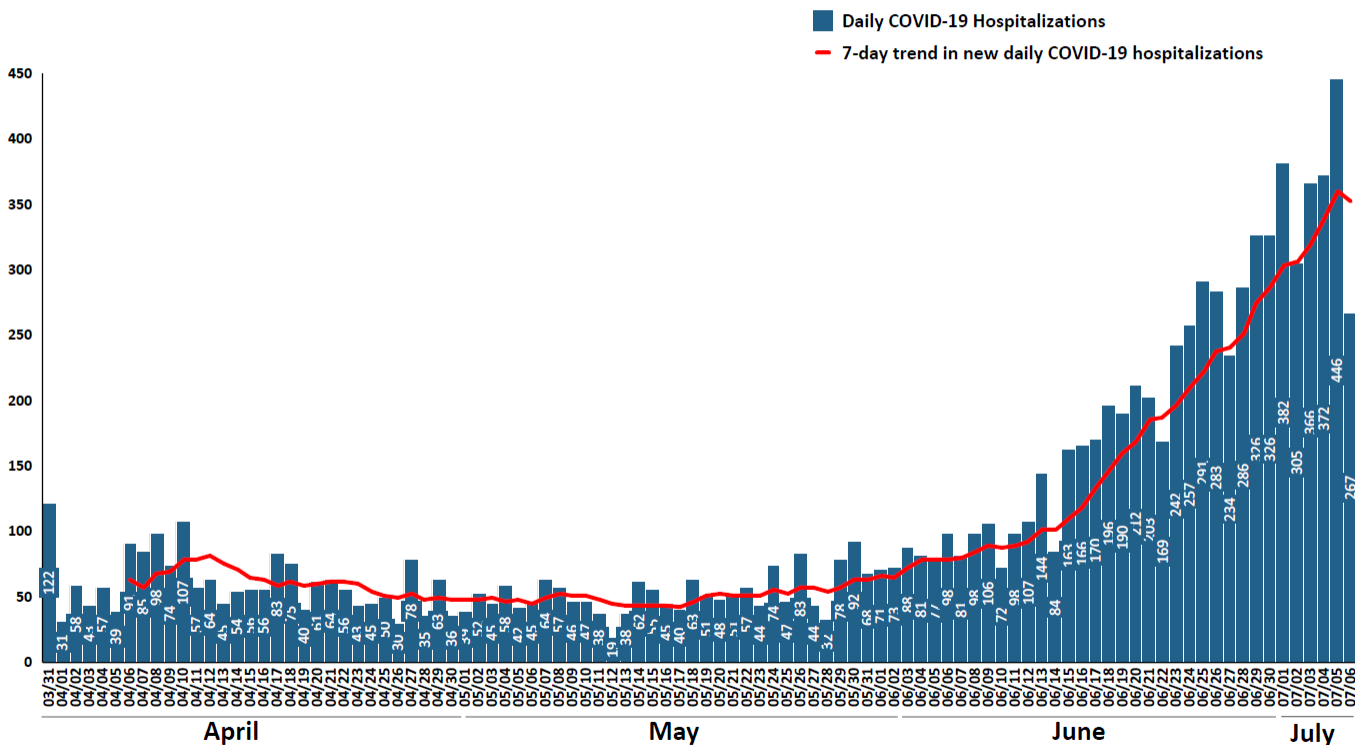
TMC DASHBOARDS

1 DAILY NEW COVID-19 CASES

July 06, 2020

TMC DAILY NEW COVID-19 HOSPITALIZATIONS

ICU & Med Surg hospitalizations



Monitoring threshold:

Threshold is exceeded by the occurrence of a positive daily growth rate, averaged over 7 days

Current status:

2.5% daily growth rate (averaged over 7 days) in the COVID-19 daily hospital admissions trend

Notes:

While new daily cases may fluctuate for a variety of reasons (e.g., testing), the daily hospitalization trend shows an objective view of how COVID-19 impacts hospital systems

Source: TMC institution clinical census

TMC TEXAS MEDICAL CENTER

"TMC" refers to the group of systems that make up Texas Medical Center

This document is solely intended to share insights and best practices rather than specific recommendations. Individual institution data is shown as reported and has not been independently verified

TMC DASHBOARDS

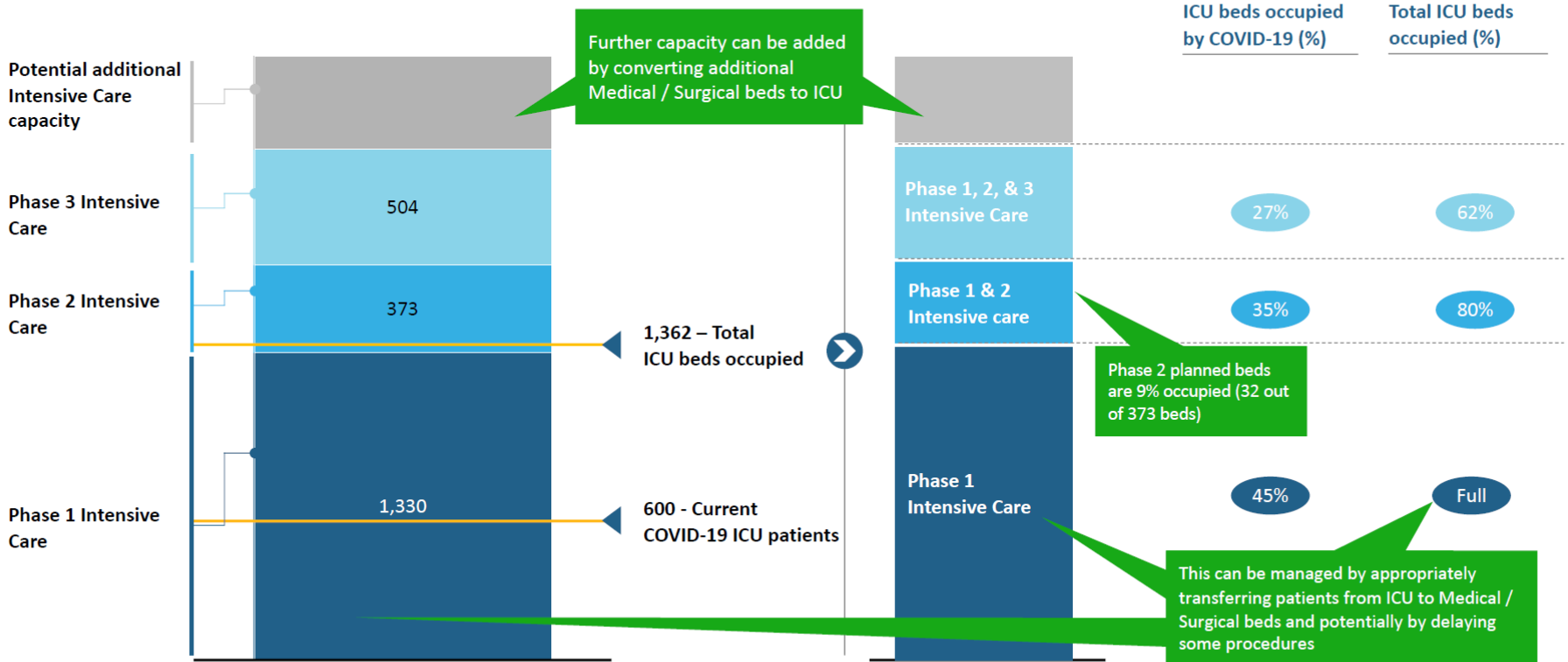
July 06, 2020

2 ICU BED OCCUPANCY

OVERVIEW OF TMC ICU BED CAPACITY AND OCCUPANCY

This capacity is actively managed by each of the hospitals and changes on a minute-by-minute basis

- Phase 1 Intensive Care capacity
- Phase 2 Intensive Care capacity
- Phase 3 Intensive Care capacity



TMC: PPE

3

TMC SYSTEM EQUIPMENT & PPE NEEDS

TMC EXPECTED PPE NEEDS

- No concern
- Moderate concern
- Warning

	<u>Average daily burn rate¹</u>	<u>Estimated days available</u>	<u>Status</u>
N95 respirator masks	8,746	162	●
Surgical face masks	133,501	139	●
Eye protection	3,620	621	●
Gowns	52,706	241	●
Gloves	827,696	31	●

July 06, 2020

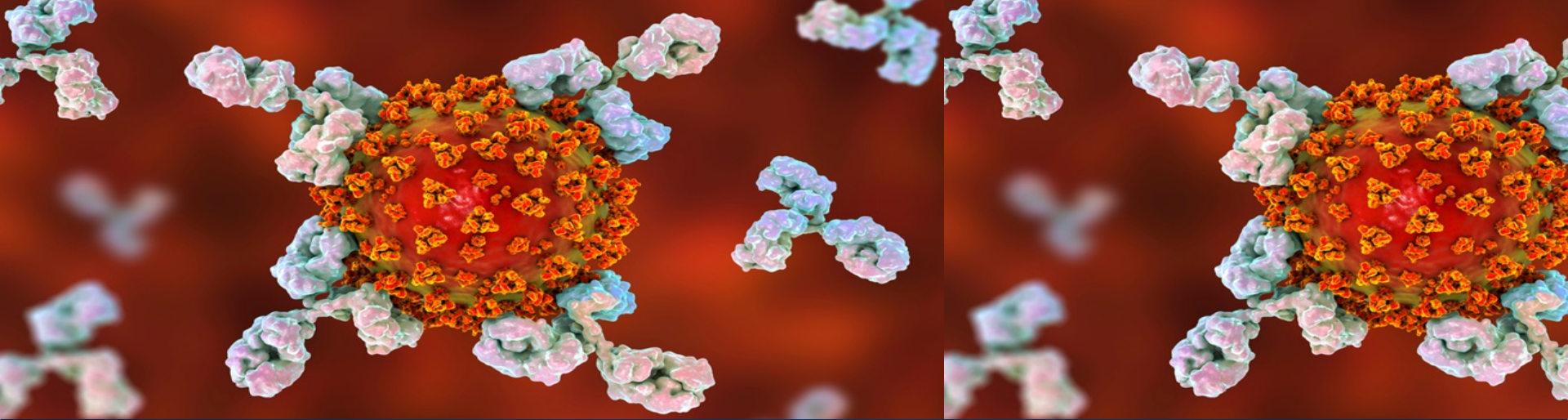
Monitoring threshold:
30-day supply of critical PPE items

Current status:
All critical PPE items within range

Note:
Data shown represents all TMC institutions and might vary from institution to institution

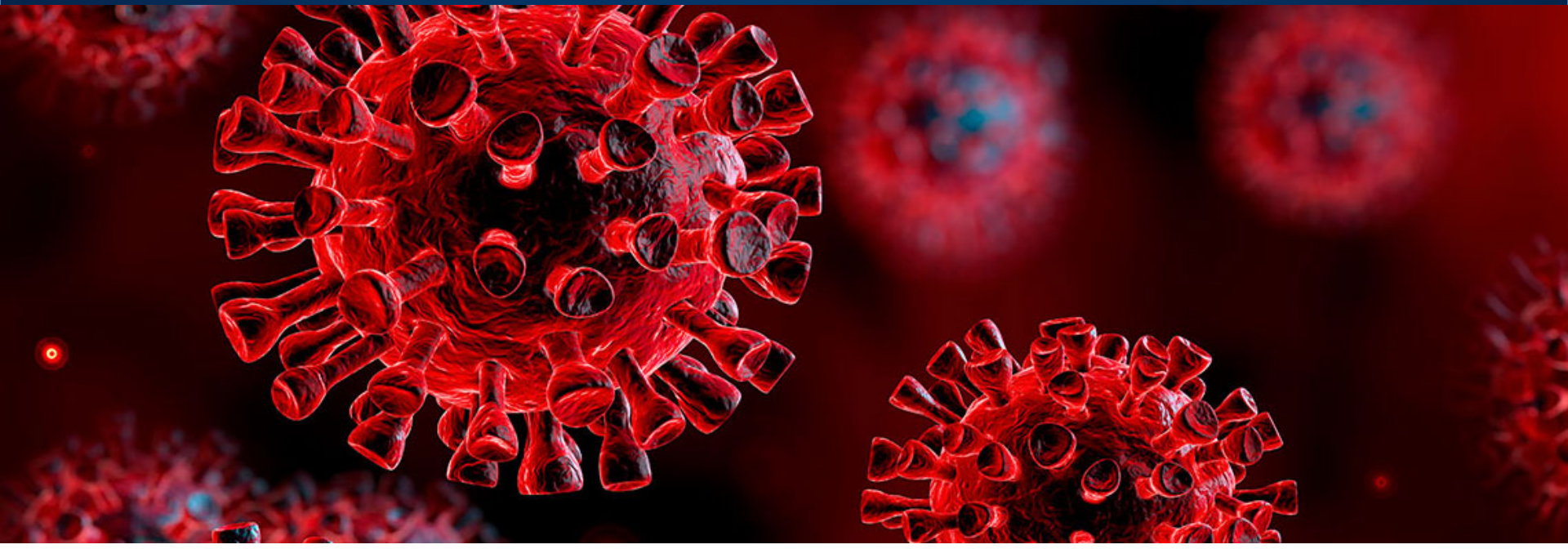
1. Calculated using trailing 2-week average burn rate

Source: Internal data collected from the systems CHI Texas Division, Harris Health System, Houston Methodist, MD Anderson Cancer Center, Memorial Hermann, Texas Children's Hospital, UTMB



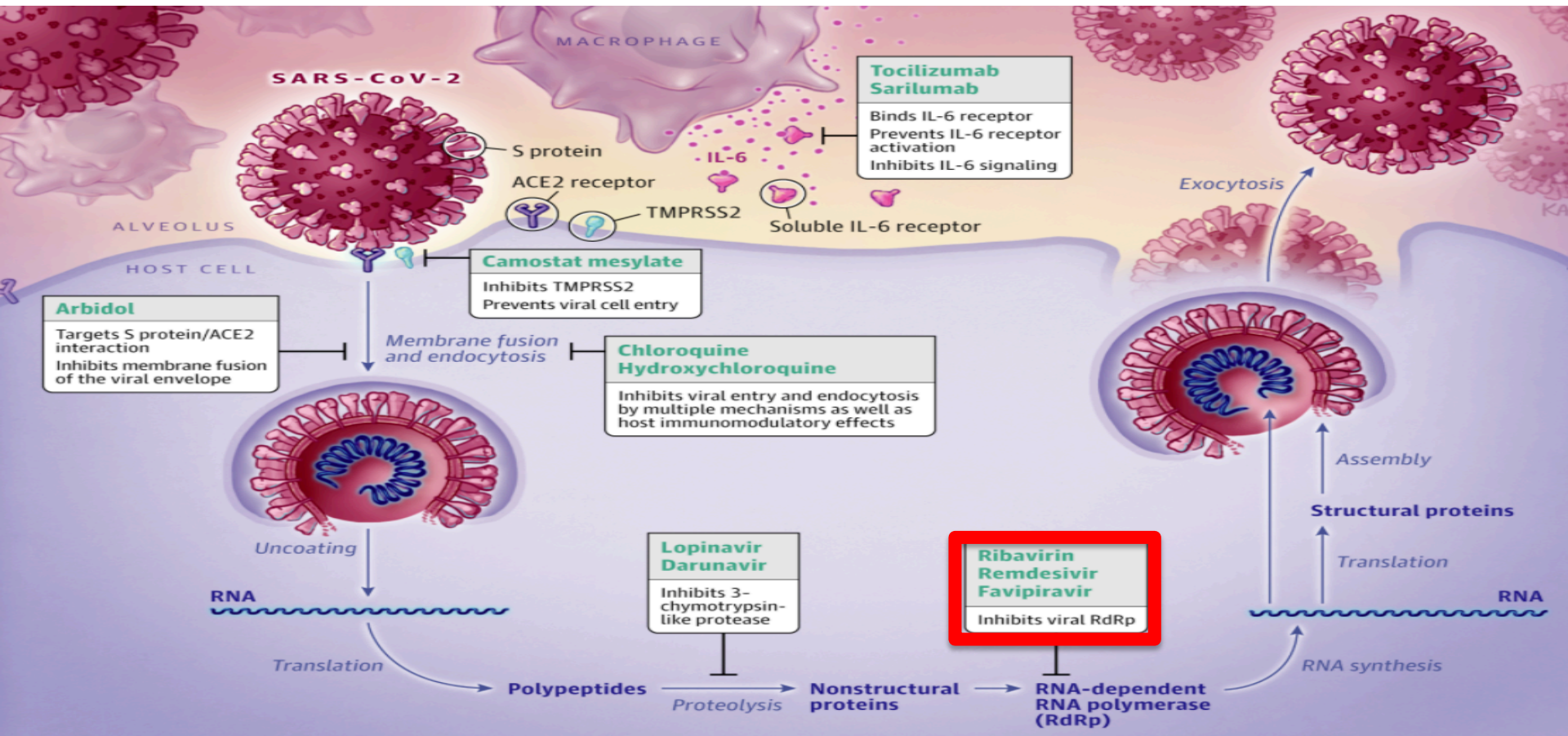
HOUSTON METHODIST ACADEMIC INSTITUTE

COVID 19 Research: Clinical Trials



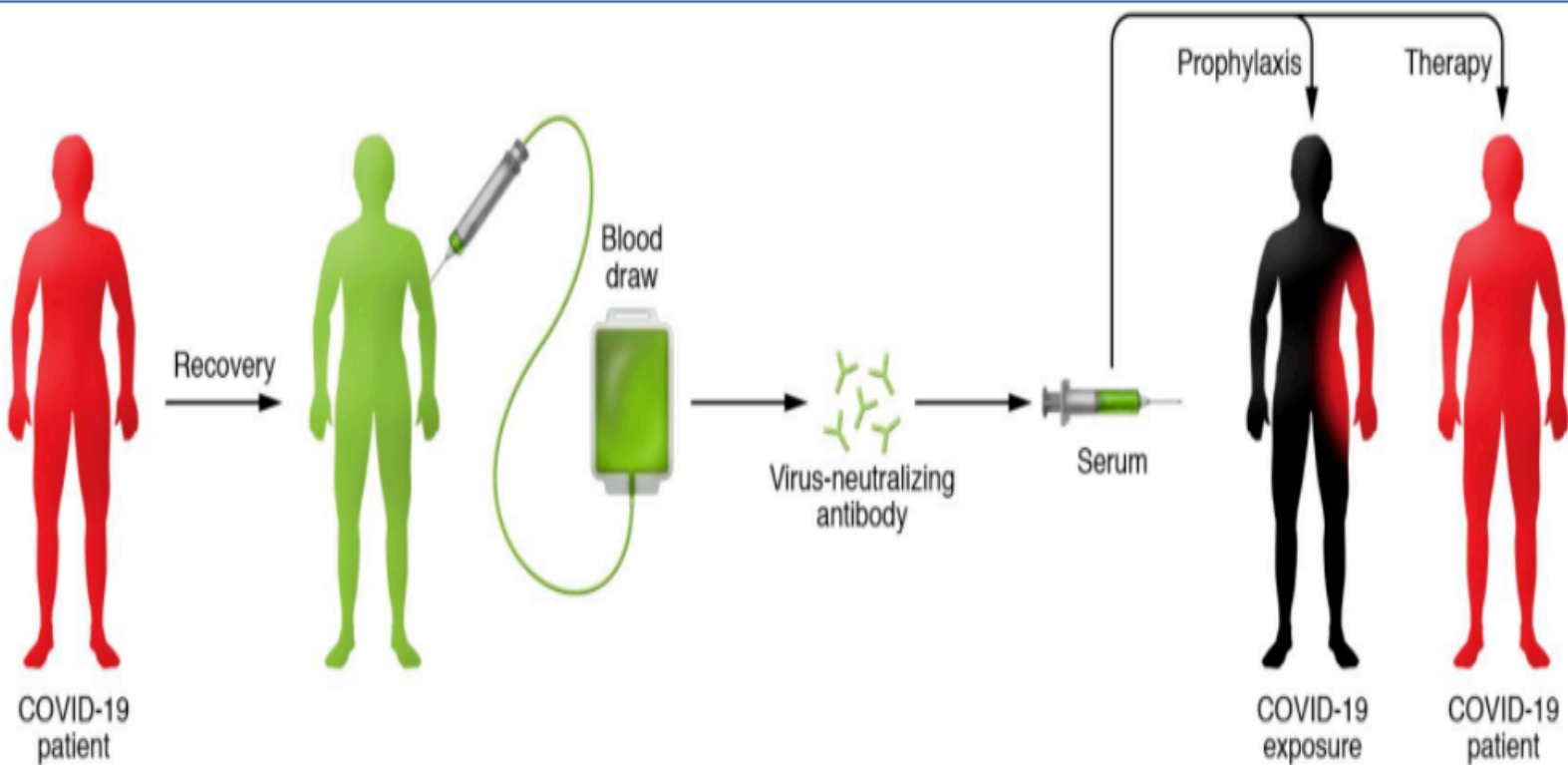
CLINICAL TRIALS - COMPLETED

- Remdesivir
 - Severely ill patients - 84 patients (71 discharged)
 - Moderately ill patients - 14 patients (14 discharged)



CLINICAL TRIALS - ONGOING

- Convalescent plasma
 - Severe life-threatening COVID-19
 - 282 patients (189 discharged)



CLINICAL TRIALS - STARTING

- Monoclonal antibodies
 - Regeneron – inpatient & outpatient
 - Lilly – outpatient

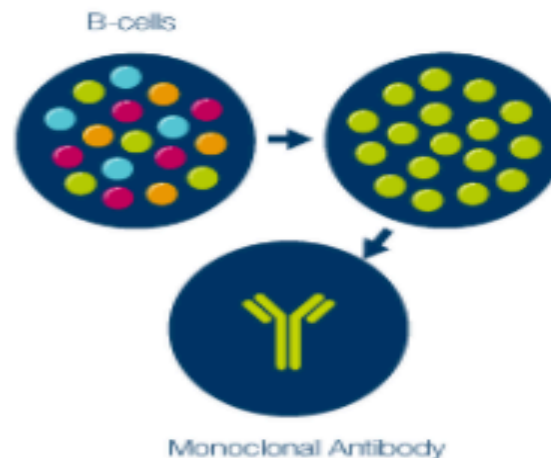
Sources for antibodies against the SARS-CoV-2 virus

- Patients who have recovered from COVID-19
- Humanised mice immunised with the SARS-Cov-2 spike protein
- Laboratory techniques such as phage display



Harnessing multiple technology platforms

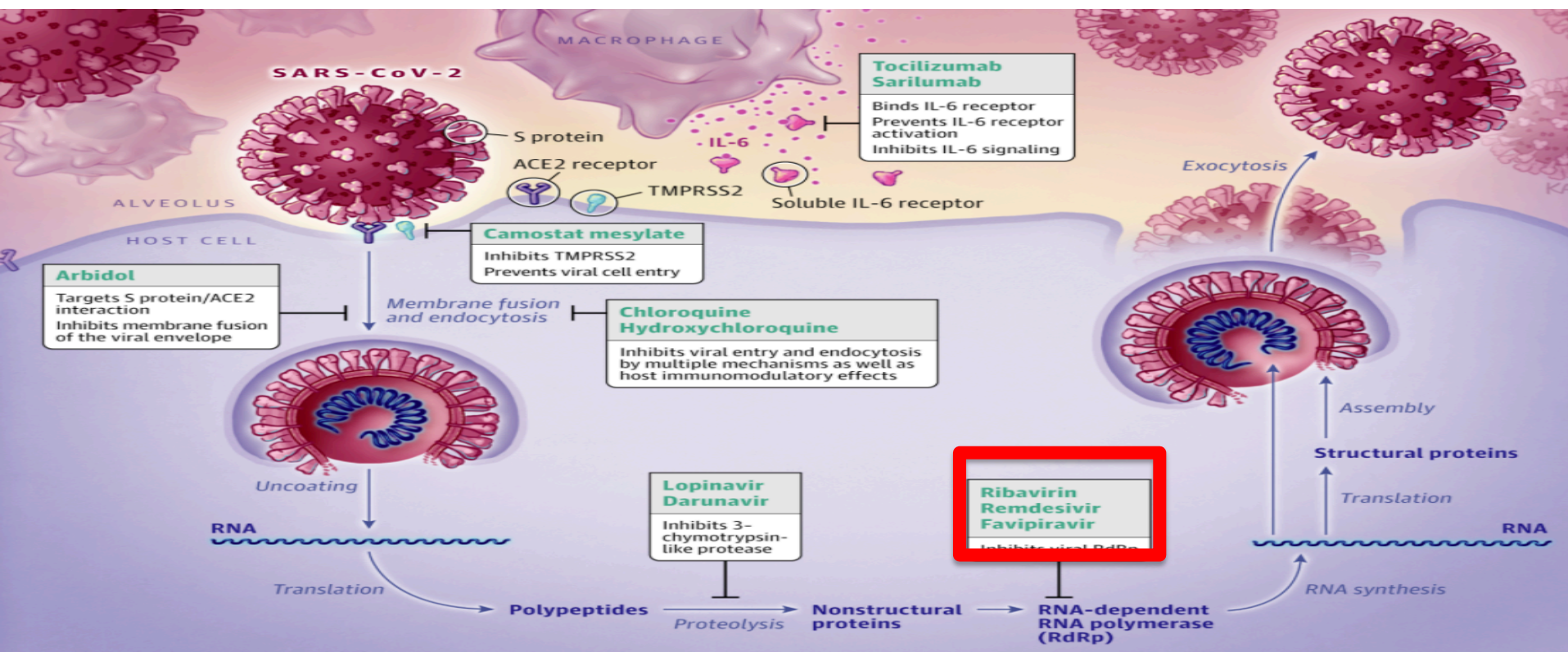
- Immune replica technology
- Hybridoma technology



Safety
and
efficacy
trials

CLINICAL TRIALS - STARTING

- Anti-viral drugs
 - Favipiravir - recruiting
 - AT-527 - in regulatory process
 - Ivermectin - recruiting
 - Potential advantage: can be given orally to outpatients



DEXAMETHASONE

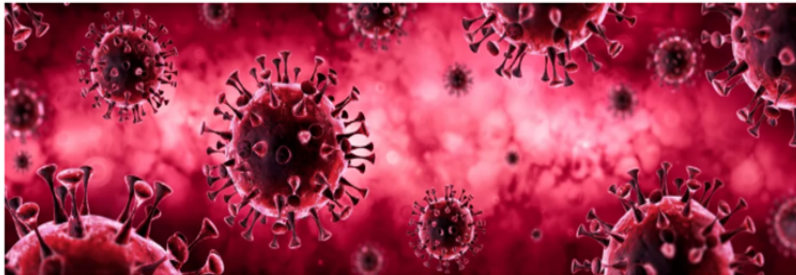
RECOVERY

Randomised Evaluation of COVID-19 Therapy

Low-cost dexamethasone reduces death by up to one third in hospitalised patients with severe respiratory complications of COVID-19

16 June 2020

Statement from the Chief Investigators of the Randomised Evaluation of COVID-19 thERapY (RECOVERY) Trial on dexamethasone, 16 June 2020



In March 2020, the RECOVERY (Randomised Evaluation of COVID-19 thERapY) trial was established as a randomised clinical trial to test a range of potential treatments for COVID-19, including low-dose dexamethasone (a steroid treatment). Over 11,500 patients have been enrolled from over 175 NHS hospitals in the UK.

On 8 June, recruitment to the dexamethasone arm was halted since, in the view of the trial Steering Committee, sufficient patients had been enrolled to establish whether or not the drug had a meaningful benefit.

- Overall mortality
21.6% vs 24.6%
(RR 0.83; $p < 0.001$)
- Reduced deaths in ventilated patients (rate ratio 0.65; $p = 0.0003$)
- Reduced death in patients receiving oxygen only (RR 0.80; $p = 0.0021$)
- No benefit among less severe (RR 1.22; $p = 0.14$)

VACCINE PROGRESS

Company	Technology Major Players	Clinical Trial Phase	Goal for EUA
Moderna/ NIAID / BARDA*	RNA	2	Fall 2020
Pfizer / BioNTech*	RNA	1 / 2	Fall 2020
Johnson & Johnson*	Viral Vector	[Phase 1 plan 9/20]	Spring 2021
Oxford / Astra Zeneca*	Viral vector	2 / 3	Fall 2020
Novavax	Protein	1	
Sanofi / Glaxo / BARDA	Protein	[Phase 1 plan 9/20]	Summer 2021
CanSino	Viral vector	1 / 2	
Sinovac	Inactivated virus	1 / 2	
Merck*	Viral vector	[Phase 1 plan 7/20]	
Innovio	DNA	1	

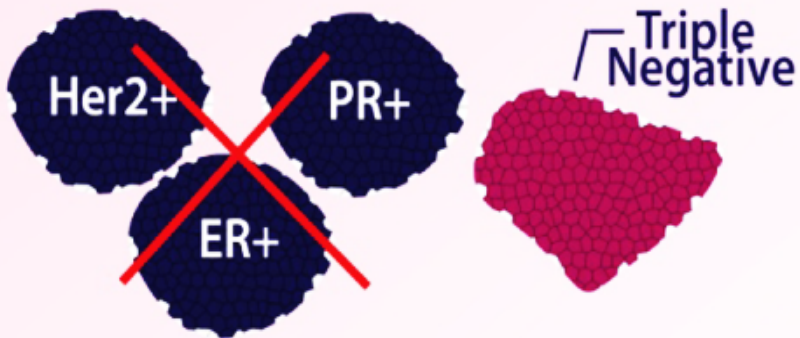
* = Warp Speed vaccine candidate

CANCER IMMUNOTHERAPY **PROJECT**

A NANO DELIVERY SYSTEM OPPORTUNITY TO
ALTER THE MICROENVIRONMENT



TRIPLE NEGATIVE BREAST CANCER (TNBC)



TNBC tumors are estrogen-receptor negative, progesterone-receptor negative and Her2-negative, meaning they do not exhibit any of these three known receptors.



1 in 8



women will be diagnosed with breast cancer in their lifetime

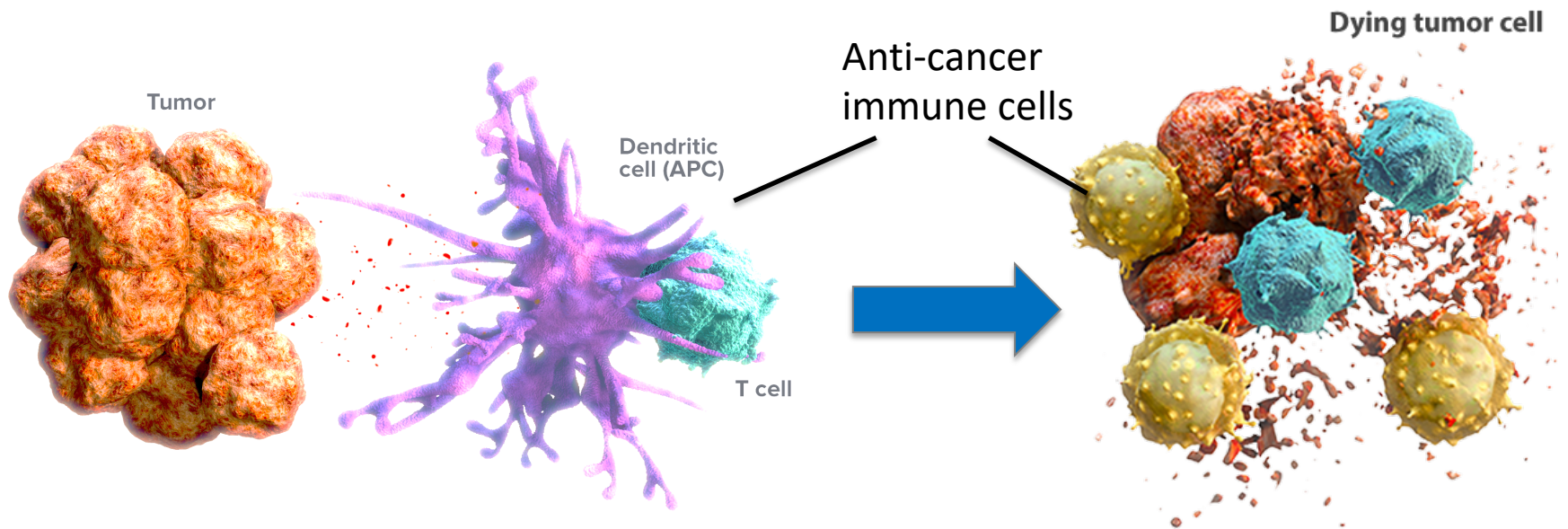


Triple negative breast cancer tends to be more aggressive, more likely to recur, and more difficult to treat than other types of breast cancer.

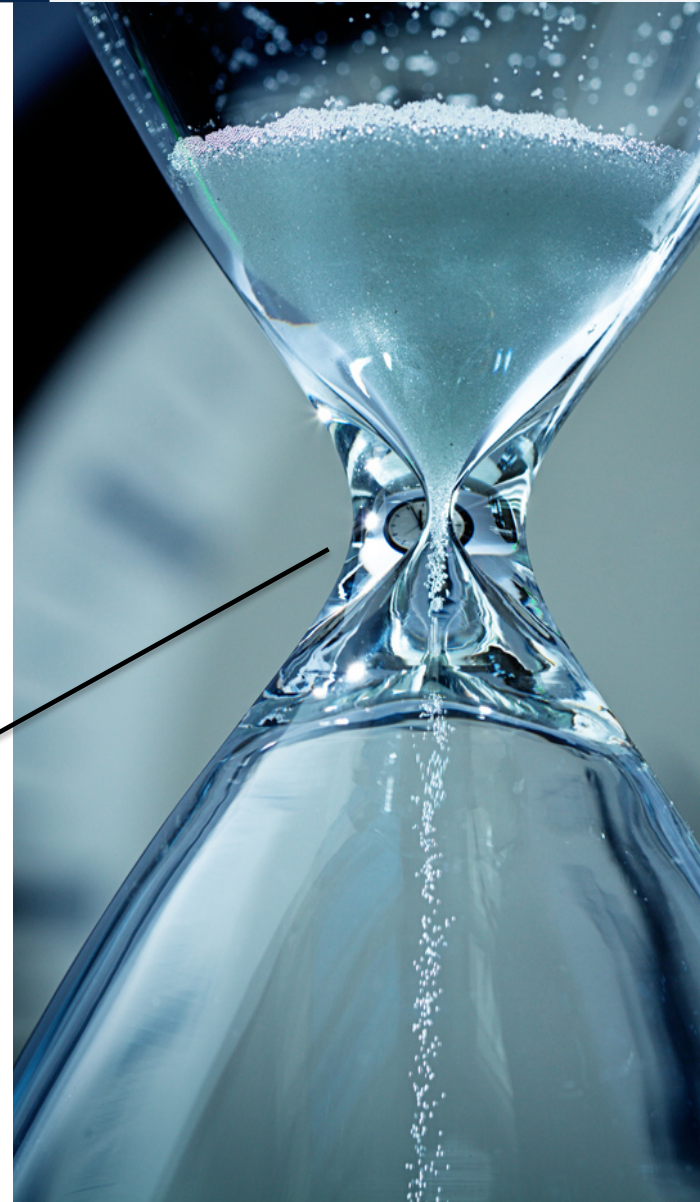
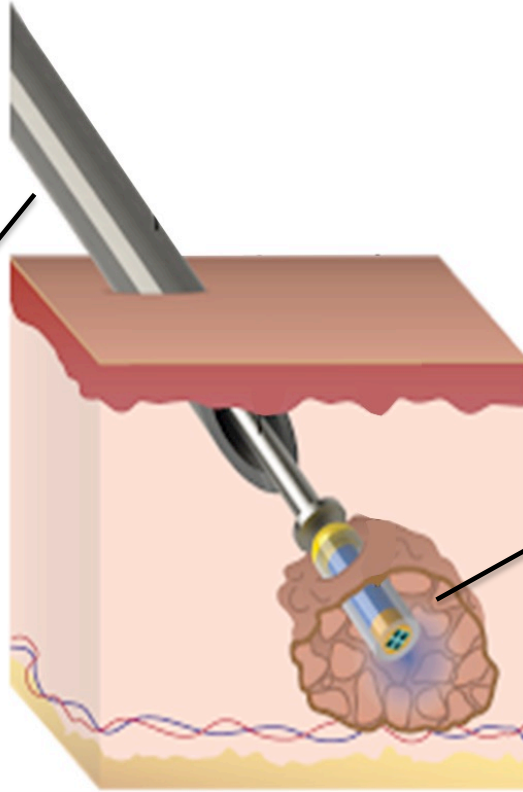
There is NO targeted therapy

IMMUNOTHERAPY

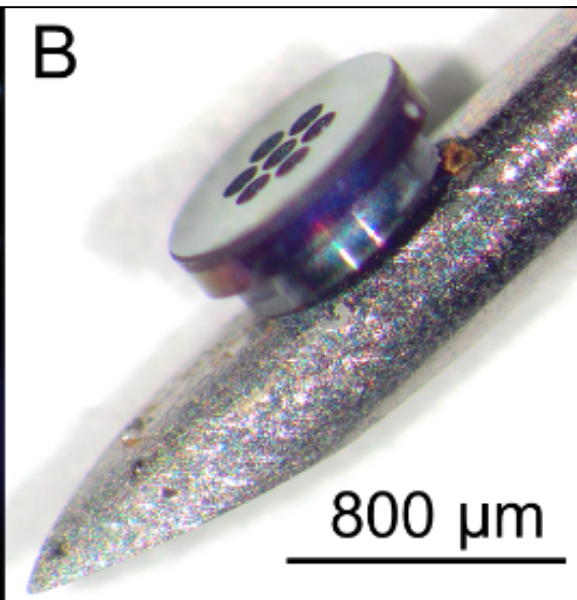
Triggers immune system to kill cancer cells



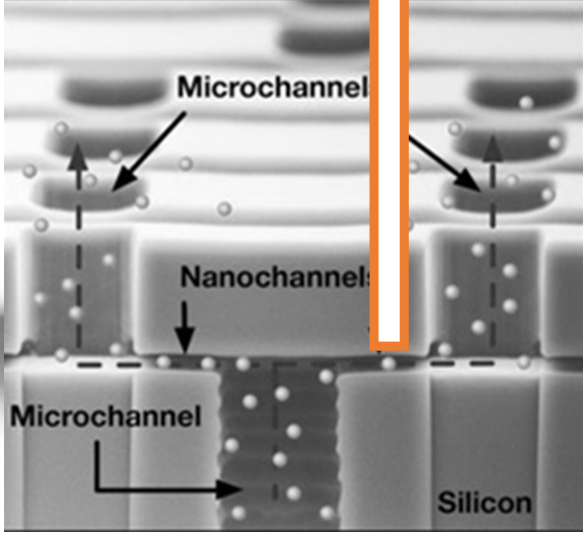
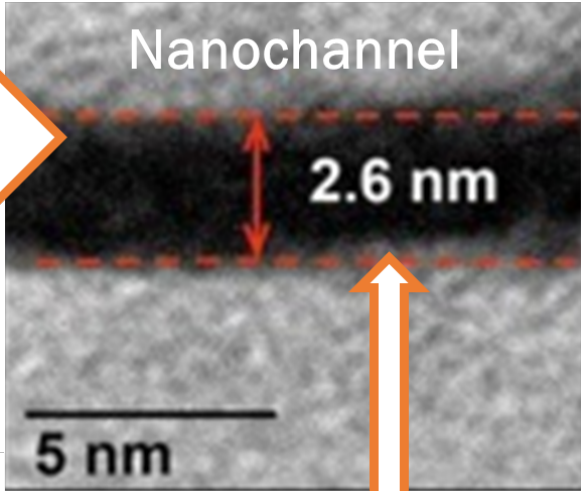
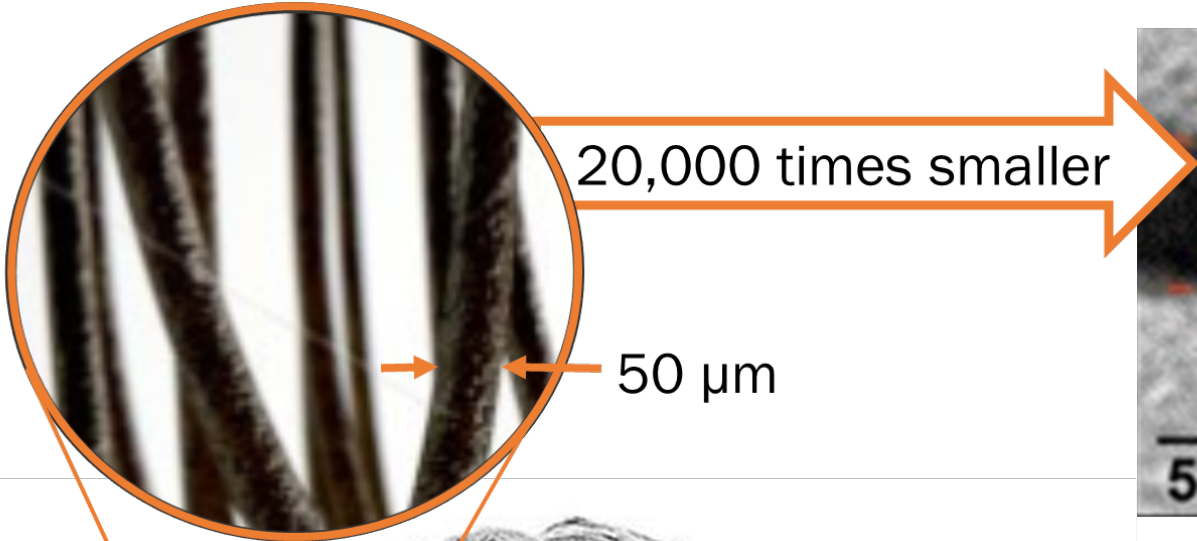
HOW DOES IT WORK?



THE NEW DEVICE

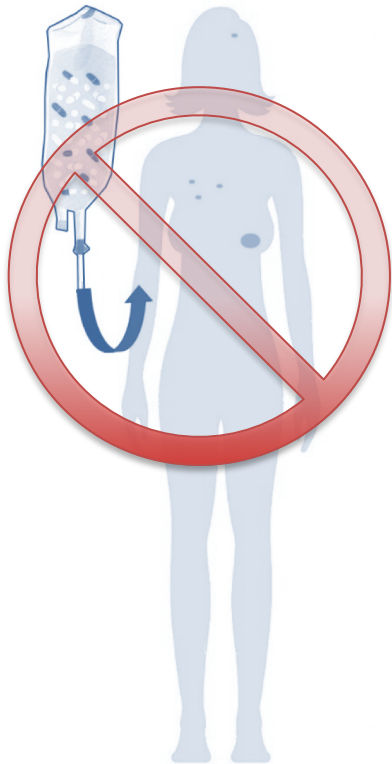


NANOCHANNELS

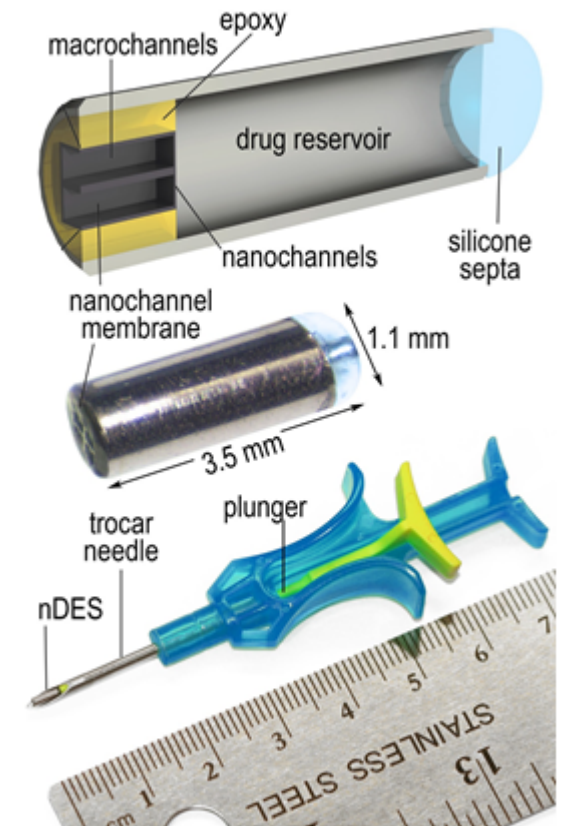
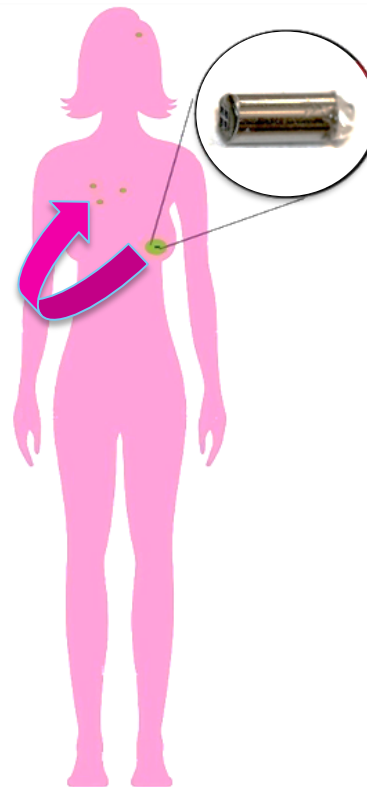


INTRATUMORAL APPROACH: NANOFLUIDIC DRUG-ELUTING SEED

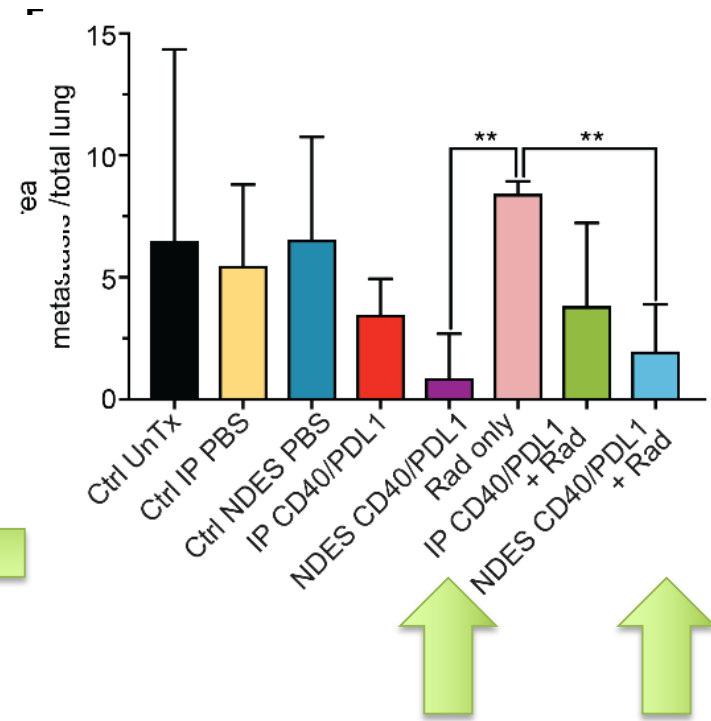
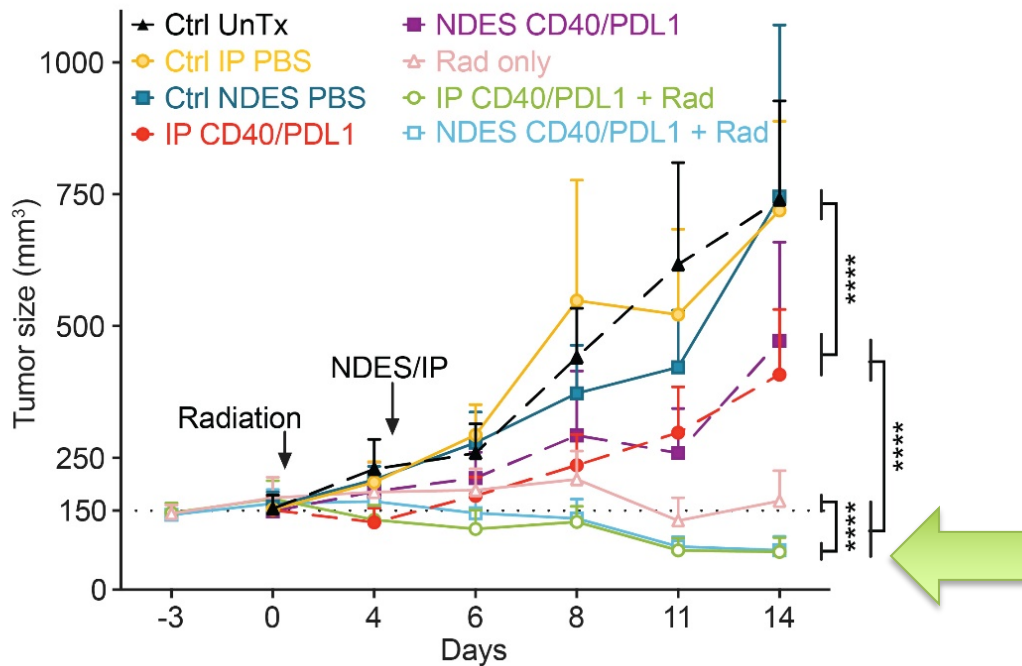
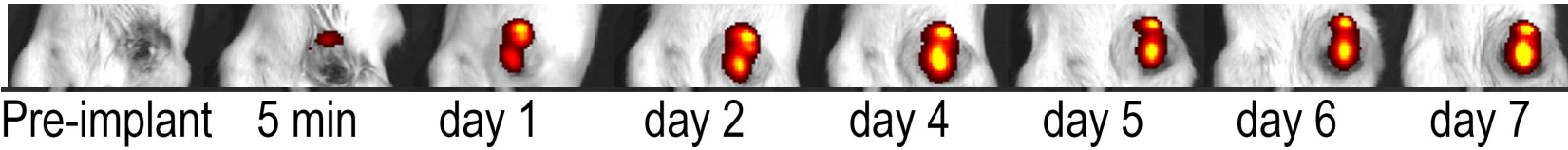
Conventional whole body
drug delivery:
ineffective and toxic



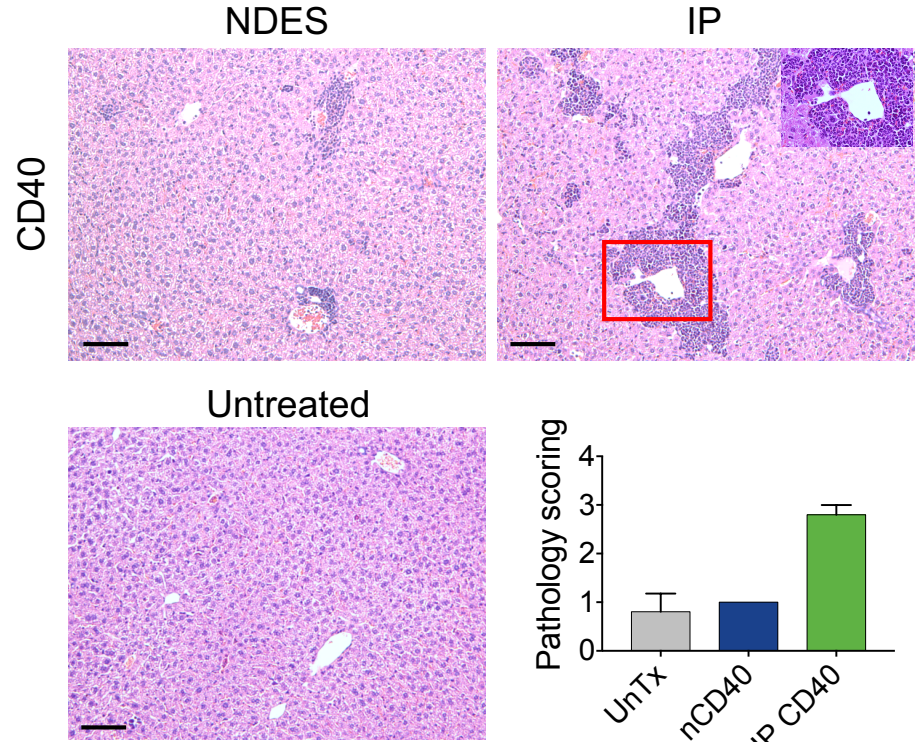
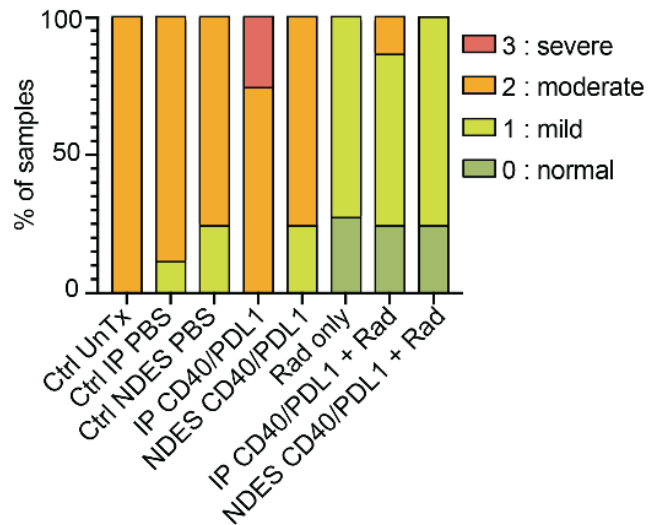
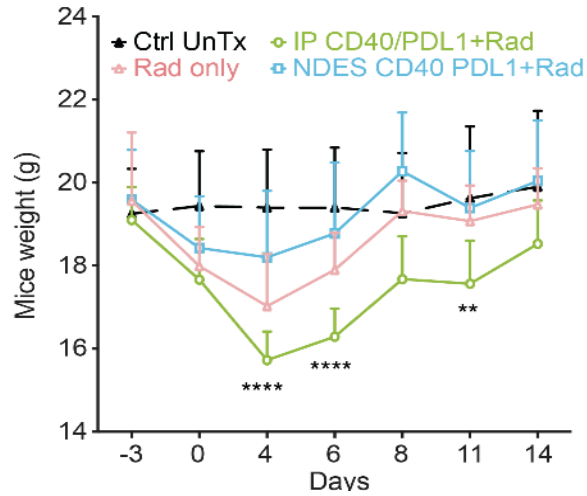
Hypothesis:
Intratumoral drug delivery:
Localized, more effective, less toxic



EFFICACY: IT NDES VS SYSTEMIC IMMUNOTHERAPY



NO ADVERSE EFFECTS



A MORE RAPID PATHWAY TO THE CLINIC



Table 3 Comparison of phase 0/microdosing with traditional phase I approaches

	Phase 0/Microdosing (eIND)	Traditional Phase I (IND)
Preclinical Package	Limited, variable; depends on extent of exposure to the test article and experimental goals	Full requirements
<i>in vitro</i> models	Full requirement	Full requirements
toxicology	Limited, variable	Full requirements
genotoxicology	None or limited	Full requirements
GMP	Flexible, depending on available preclinical information and route of administration (e.g., sterility ensured for IV route)	Full requirements
Regulatory Review	30-day	30-day
Usual Duration of Program	4-12 months	12-24 months
Cost of Program	\$ 0.5-0.75 M	\$ 1.5-2.5 M
Studies size (typical)	4-10 participants	6-30 participants

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MEDICAL RESEARCH IN SPACE



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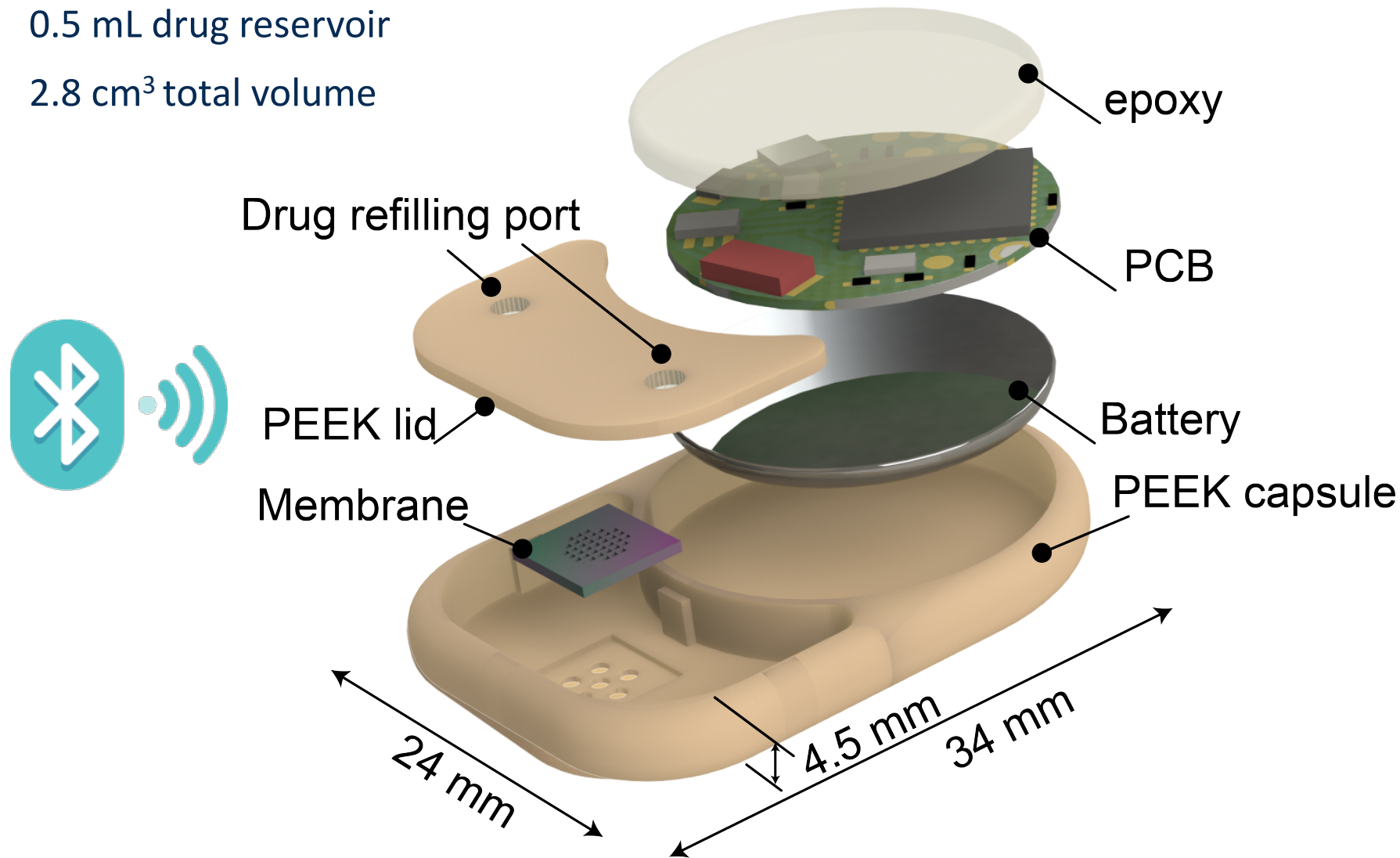
REMOTELY CONTROLLED DRUG DELIVERY IMPLANT



REMOTELY CONTROLLED DRUG DELIVERY IMPLANT

0.5 mL drug reservoir

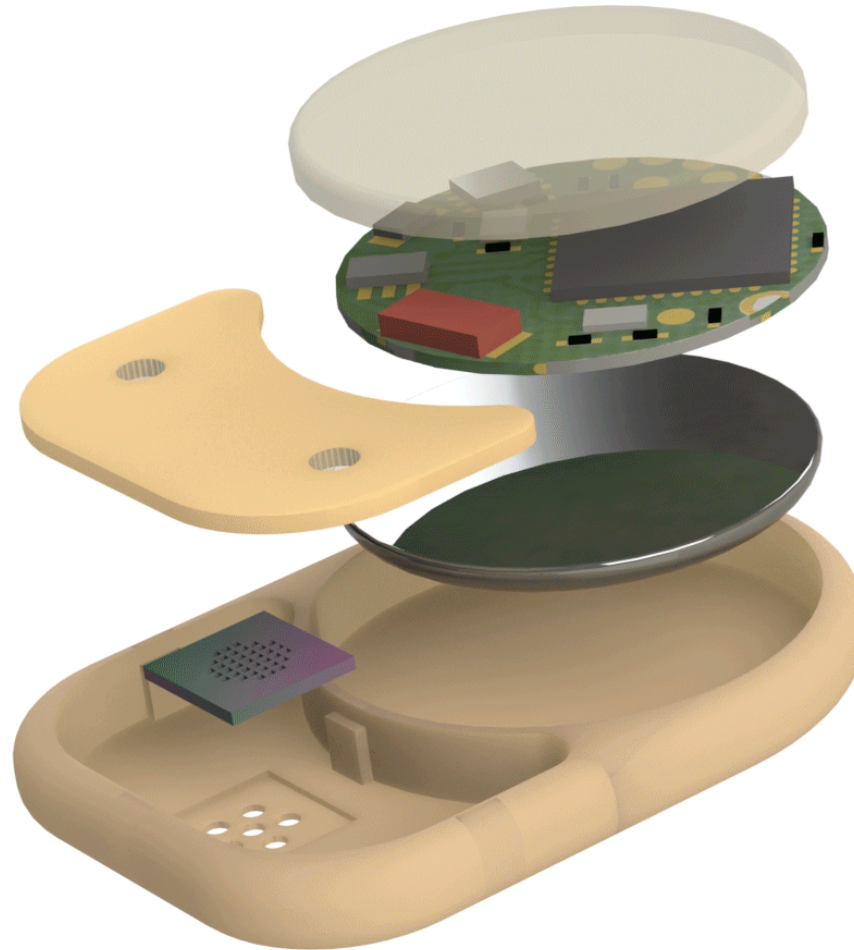
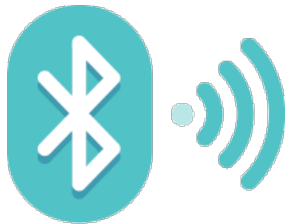
2.8 cm³ total volume



REMOTELY CONTROLLED DRUG DELIVERY IMPLANT

0.5 mL drug reservoir

2.8 cm³ total volume



CANCER TELEMEDICINE?

Device status

System state: Up and running

RESET

MAC	RSSI	Status	Last discovered
20:D2:84	-74	10	06/Nov/17 18:28:06
20:D2:B3	-83	10	06/Nov/17 18:28:06
27:07:8D	-92	10	06/Nov/17 18:28:06
27:0B:D7	-62	10	06/Nov/17 18:28:06
27:0F:11	-53	10	06/Nov/17 18:28:06

Edit device status

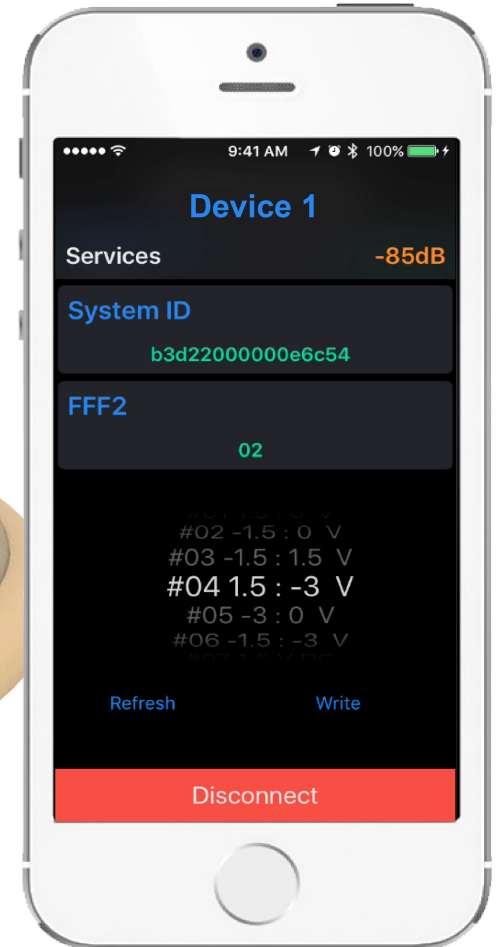
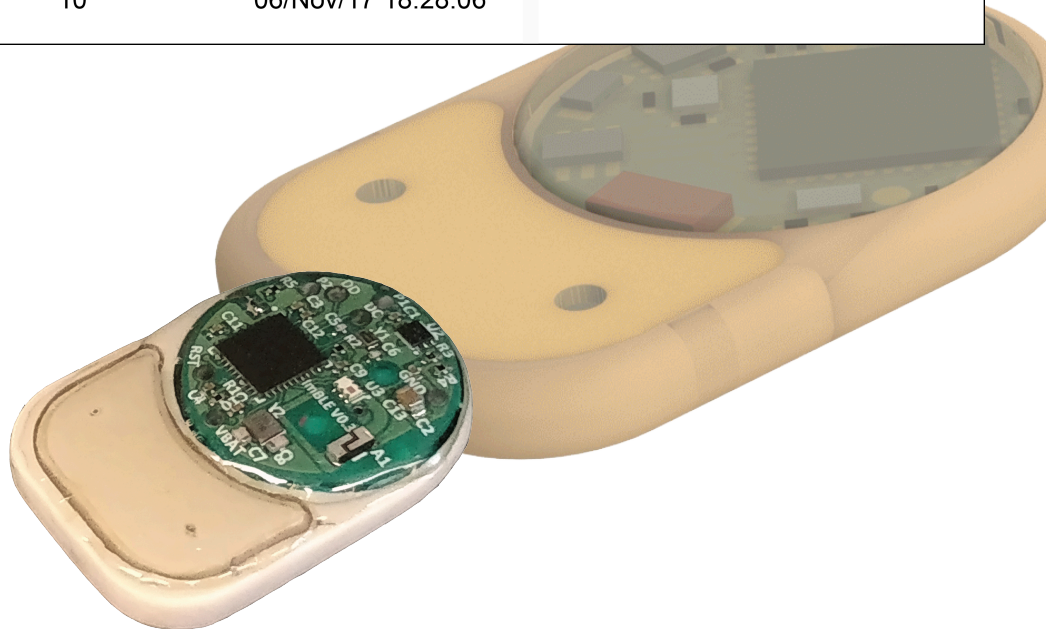
27:0F:11 ▼

Device status: #10 OFF

READ

#10 OFF ▼

WRITE



NEW IMPLANTS MATERIALS IN MICROGRAVITY

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October 19th 2019
Evaluation of Lamborghini
Carbon Fiber Materials on
the International Space
Station



THE GRATTONI LAB

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Thank you Nancy Owens Breast Cancer Foundation!